

REMARKS

Claims 1, 4 and 5 are pending. Claims 2, 3 and 6-20 have been cancelled without prejudice. Applicants reserve the right to pursue the cancelled subject matter in future divisional or continuation applications.

Claim 1 has been amended to include the subject matter of claims 2 and 3. In view thereof claims 2 and 3 have been cancelled and the dependency of claim 4 has been amended.

Claims 1 has also been editorially amended.

No issues of new matter should arise and entry of the amendment is respectfully requested.

I. Rejection under 35 USC §112, First Paragraph

Claims 1-5 are rejected under 35 USC 112, first paragraph, as not being enabled for treating a blood disorder.

Claim 1 has been amended to delete a blood disorder and hence the rejection is now moot. As noted by the Examiner the specification is enabling for treating sickle cell anemia and thalassemia. In view thereof, withdrawal of this rejection is respectfully requested.

II. First Rejection under 35 USC §112, Second Paragraph

Claims 2-5, 7-10, 12-15 and 17-20 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to specify the term “therapeutic agent”.

The Examiner asserts that the claims for failing to specify the term “therapeutic agent”. The term therapeutic agent and claims 2, 7, 12 and 17 have been cancelled. In view thereof, withdrawal of this rejection is respectfully requested.

III. Second Rejection under 35 USC §112, Second Paragraph

Claims 1-20 are rejected under 35 USC 112, second paragraph, as being incomplete.

The Examiner asserts that claims 1-10, 11-15 and 16-20 fail to provide a subject for the verb “administering”. Claim 1 has been editorially amended to include the language “to a patient in need thereof”. In view thereof, withdrawal of this rejection is respectfully requested.

IV. First Rejection under 35 U.S.C. §103

Claims 1 and 2 are rejected under 35 U.S.C. §103 as being unpatentable over Pinsky et al (US 6,316,403).

Applicants respectfully traverse the rejection and respectfully submit that the claimed invention is unobvious over the cited reference.

The pending claims are directed to the treatment of sickle cell anemia or thalassemia comprising administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate and at least one antioxidant.

Pinsky is cited by the Examiner for the treatment of ischemic disorders, such as sickle cell anemia, using a composition comprising P-selectin antagonists, such as a nitric oxide precursor, in combination with a therapeutic agent such as a tissue plasminogen activator. Applicants respectfully submit that nowhere in the teachings of Pinsky is there any mention of the use of an **antioxidant** (emphasis added) either alone or in combination with a nitric oxide donor for the treatment of ischemic disorders, such as sickle cell anemia. Hence Pinsky is not analogous art. Additionally there is no suggestion or motivation by Pinsky to treat ischemic disorders, such as sickle cell anemia by administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with an antioxidant.

Therefore Applicants respectfully submit that the cited reference does not disclose or suggest, or provide motivation one to arrive at the presently claimed invention. In view thereof, Applicants submit claims 1 and 2 are patentable over Pinsky and withdrawal of this rejection is respectfully requested.

V. Second Rejection under 35 U.S.C. §103

Claims 3-5 are rejected under 35 U.S.C. §103 as being unpatentable over Pinsky et al (US 6,316,403) in view of Loscalzo et al (WO 02/34303).

Applicants respectfully traverse the rejection and respectfully submit that the claimed invention is unobvious over the cited references and there is no motivation to combine the cited references to arrive at the presently claimed invention. Applicants respectfully submit that the cited references, individually or in combination, do not disclose or suggest, or provide motivation to arrive at the presently claimed invention.

The pending claims are directed to the treatment of sickle cell anemia or thalassemia comprising administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate and at least one antioxidant.

As noted above, and by the Examiner in the Office Action at page 8 line 21 to page 9, line 2, the teachings of Pinsky **do not** disclose a nitric oxide donor such as N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with an antioxidant for the treatment of sickle cell anemia or thalassemia.

Loscalzo is cited by the Examiner for teaching methods of treating vascular diseases due to nitric oxide insufficiency using an antioxidant and a nitric oxide donor. Applicants respectfully submit that Loscalzo does not disclose the treatment of blood disorders. Additionally the vascular diseases disclosed by Loscalzo are very different from the blood disorders of the present invention. Moreover there is no suggestion or motivation by Loscalzo to treat blood disorders, such as sickle cell anemia by administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with an antioxidant.

As mentioned above, Pinsky does not disclose the methods of the present invention. Additionally, there is no motivation in Pinsky for one to administer an antioxidant for the treatment of diseases or disorders. Pinsky, taken alone, does not render the claimed invention obvious.

Loscalzo does not cure the deficiencies of Pinsky. Loscalzo does not provide any motivation or suggestion to modify Pinsky to arrive at the claimed invention. In view thereof, Pinsky in combination with Loscalzo does not motivate one to arrive at the present invention.

In view thereof, Applicants respectfully submit that the claims of the present invention are unobvious over the cited references, alone and in combination, and respectfully request the rejection under 35 U.S.C. §103(a) be withdrawn.

VI. Third Rejection under 35 U.S.C. §103

Claims 6-10 are rejected under 35 U.S.C. §103 as being unpatentable over Pinsky et al (US 6,316,403) in view of Loscalzo et al (WO 02/34303).

Claims 6-20 have been cancelled in the pending application. In view thereof, withdrawal of this rejection is respectfully requested.

VII. Fourth Rejection under 35 U.S.C. §103

Claims 11-15 are rejected under 35 U.S.C. §103 as being unpatentable over Loscalzo et al (WO 02/34303) in view of Pinsky et al (US 6,316,403) in combination with Bandaru et al (US Publication No. 2003/0064439)

Claims 11-15 have been cancelled in the pending application. In view thereof, withdrawal of this rejection is respectfully requested.

VIII. Fifth Rejection under 35 U.S.C. §103

Claims 16-20 are rejected under 35 U.S.C. §103 as being unpatentable over Pinsky et al (US 6,316,403) in view of Loscalzo et al (WO 02/34303).

Claims 16-20 have been cancelled in the pending application. In view thereof, withdrawal of this rejection is respectfully requested.

IX. Conclusion

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 08-0219, under Order No. 0102258.00375US2 from which the undersigned is authorized to draw.

Respectfully submitted,

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